PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	GUIDELINES AND ANTIMICROBIAL RESISTANCE: A SYSTEMATIC REVIEW ON NATIONAL RECOMMENDATIONS ON THE USE OF ANTIBIOTICS ACROSS UN MEMBER STATES
AUTHORS	ELIAS, Christelle; MOJA, Lorenzo; Mertz, Dominik; Loeb, Mark; FORTE, Gilles; MAGRINI, Nicola

VERSION 1 - REVIEW

REVIEWER	David Lye Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital; Yong Loo Lin School of Medicine, National University of Singapore; Lee Kong Chian School of Medicine, Nanyang Technological University; Singapore
REVIEW RETURNED	14-Mar-2017

GENERAL COMMENTS	This is a timely and relevant study of the inclusion of local resistance data to guide empiric antibiotic recommendations in five common infectious disease syndromes. My main concern is technically this is a systematic review but the authors have called it a cross-sectional study. PRISMA is the reporting guideline for systematic review. I have a few minor inputs for the authors to consider: (1) The authors should list search times instead of saying "variations" (line 109) (2) Only one author reviewed each guideline. More than one person reduces bias. It is unclear how with one reviewer per guideline, "different patterns were collegially discussed". (3) In table 2, the year of publication need not be reported as median, min and max. This information can be reported in text. (4) In table 4, "AERU" is not an intuitive acronym for Pseudomonas aeruginosa. (5) In line 253 in Discussion, there was a mention of "less than 10%". However I cannot find the source of this information in Results. (6) In line 291, "UTI's" may be a mistake as the authors may be referring to upper respiratory tract infections.

REVIEWER	Tommaso Cai Department of Urology, Santa Chiara Regional Hospital, Trento, Italy.
REVIEW RETURNED	25-Mar-2017

GENERAL COMMENTS	The paper is well done and very interesting.

	I have only this minor comment: - please add few sentences or comments about the role of antibiotic prophylaxis in the field of antibiotic stewardship. This aspect is very important to highlight.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

This is a timely and relevant study of the inclusion of local resistance data to guide empiric antibiotic recommendations in five common infectious disease syndromes.

My main concern is technically this is a systematic review but the authors have called it a cross-sectional study. PRISMA is the reporting guideline for systematic review.

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Thank you for this comment. We added a PRISMA checklist as a research checklist.

We agree to consider this study as a systematic review. Therefore we removed the words “cross-sectional” in the methods paragraph.

I have a few minor inputs for the authors to consider:

(1) The authors should list search times instead of saying "variations" (line 109)

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Thank you for your suggestion. We replaced the word “variations” by the terms we used in Medline to screen guidelines. For clinical practice guidelines we searched for “clinical practice guideline*” or “guideline*”. For the name of the syndrome, we illustrated our screening with an example. For instance, to look for community-acquired pneumonia guidelines, we searched for “pneumonia” or “community acquired pneumonia” or “respiratory tract infection” or “lower respiratory tract infection”.

(2) Only one author reviewed each guideline. More than one person reduces bias. It is unclear how with one reviewer per guideline, "different patterns were collegially discussed".

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One author screened guidelines and performed data collection and analysis. We agree that searches done in duplicate might have reduced bias of our study. However in our study, our inclusion criteria were relatively straightforward, and we did not have to extract numbers relative to the effect of the intervention and control, such as in Cochrane reviews. The researcher who reviewed guidelines exposed and shared doubts and hesitations concerning the observed resistance patterns for each syndrome with infectious diseases experts. For this reason, we think that the risk of errors is minimal. Nevertheless, we acknowledged this point as a main limitation of our study, clearly stating in the discussion:

“We recognize that our study can provide nothing more than a snapshot of the current state of the recommendations related to one dimension, antibiotic resistance. Comprehensive user-centered evaluations of the overall quality of guideline are needed. It was not our aim to assess whether recommendations have improved or worsened over time. Rather we sought to assess whether a problem existed at the time of our study. We did not investigate if recommendations on discrete resistance patterns were correct, or supported by evidence. The relevance of resistance patterns was not weighted. We accepted study authors’ guidance on discrete patterns at face value, without further evaluating the quality of the recommendation. We adopted a non-validated arbitrary ordinal scale. Searches were done by a single researcher. We did not consider paper-based guidelines, which might be still prevalent in some contexts. Further research on the quality and relevance of specific recommendations based on resistance is needed identifying further obstacles to progress AMR and bringing them to light.”

(3) In table 2, the year of publication need not be reported as median, min and max. This information can be reported in text.
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In Table 2, we removed the line concerning the year of publication. This information was already mentioned in the text "Half of the CPGs were published between 2011 and 2016".

(4) In table 4, "AERU" is not an intuitive acronym for Pseudomonas aeruginosa.
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Thank you for your suggestion. We replaced the acronym “Aeru risk” with “Pseudomonas risk” in Table 4, as well as in the Supplementary Table 1. Captions were also modified accordingly.

(5) In line 253 in Discussion, there was a mention of "less than 10%". However I cannot find the source of this information in Results.
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The result “less than 10%” refers to the 6.4% of satisfactory recommendations. We revise the statement to clarify to which finding we are referring:
“Moreover, of the 251 recommendations, fewer than one in ten consistently reported data on their country specific resistance patterns.”

(6) In line 291, "UTI's" may be a mistake as the authors may be referring to upper respiratory tract infections.
In this sentence we referred to Urinary Tract Infections. However, to be consistent with the results presented in our study (Table 4), we edited and clarified this sentence by comparing the limited amount of patterns in Upper respiratory tract infections and urinary tract infections with CAP’s resistance patterns.

Reviewer 2
The paper is well done and very interesting.
I have only this minor comment:
Please add few sentences or comments about the role of antibiotic prophylaxis in the field of antibiotic stewardship. This aspect is very important to highlight.
Thank you for your revision and suggestions. Indeed, the role of antibiotic prophylaxis is the field of antimicrobial stewardship is substantial. We added the following statements in the discussion:
“ National and international recommendations should be accompanied by facility-specific antibiotic recommendations, particularly for common syndromes. Among the others, surgical prophylaxis has an important role as target of local stewardship programs. Most guidelines recommend a maximum postoperative duration of surgical antibiotic prophylaxis of 24 hours, but increasing evidence shows that using only a single preoperative dose (and possible additional intraoperative doses according to the duration of the operation) might be equally effective [32]. Prophylaxis use should be risk-adjusted according to surgical procedures to ensure that harms in terms of bacterial resistance do not outweigh the benefits. Implementation of a monitored antibiotic policies results in lower total antibiotic consumption, reduced antibiotic resistance, and reduced costs without increasing the risk of postoperative infections [33] “
32 Allegranzi B, Bischoff P, de Jonge S, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis 2016;16:276–87. doi:10.1016/S1473-3099(16)30398-X
33 Cai T, Verze P, Brugnolli A, et al. Adherence to European Association of Urology Guidelines on Prophylactic Antibiotics : An Important Step in Antimicrobial Stewardship. Eur Urol 2016;69:276–83. doi:10.1016/j.eururo.2015.05.010

additional requests

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The supplementary tables has been referenced in the text. "Of all recommendations, alternative antibiotic therapy was observed for all syndromes where fluoroquinolones appeared to be the most frequent alternative antibiotic in CAP (11%) and UTIs (12.7%) (Suppl. Table 1 and 2)."

VERSION 2 – REVIEW

REVIEWER	David Lye Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital, Singapore
REVIEW RETURNED	16-Apr-2017

GENERAL COMMENTS	I am satisfied with the revisions.